Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-7. (Canceled)

8. (Currently Amended) A method for designing an antisense oligonucleotide sequence for a target mRNA or its precursor comprising the steps of:

(a) selecting all pairs of sequences on the target mRNA, or its precursor, complementary to each other and separated by at least three nucleotides, but without independently selecting pairs of sequences which are shorter than, and composed of nucleotides of, the selected sequences;

(b) assigning a numerical value to each pair that reflects the possibility of forming a complementary double-stranded region between said pair of sequences based upon the distance between said pair of sequences and the bond energy ΔG for said pair of sequences, wherein a lower numerical value indicates a lower possibility, and wherein the numerical value increases with an increase in said bond energy and the value decreases with an increase in the distance between said paired sequences;

(c) assigning the numerical ~~value~~ values obtained in step (b) to each nucleotide of each of the paired sequences;

(d) summing the numerical values, which are assigned in step (c) for all pairs of sequences selected in step (a), for each nucleotide in the target mRNA or its precursor;

(e) selecting one or more regions each of which ~~consist~~ consists of at least 6 contiguous nucleotides and ~~have~~ has a low summed value relative to another region; and

(f) designing [[an]] one or more antisense ~~oligonucleotide~~ oligonucleotides, wherein each oligonucleotide is complementary to ~~said~~ a region selected in step (e).

9. (Previously Presented) The method of claim 8, wherein said bond energy for forming the complementary double-stranded region is determined by the nearest neighbor model.

10. (Currently Amended) The method of claim 8, wherein said step (a) is conducted by the steps:

~~(a)~~ (g) selecting a first sequence consisting of 2 or more nucleotides from the target mRNA or its precursor;

~~(b)~~ (h) selecting a second sequence that is complementary to the first sequence and is separated by at least three nucleotides from the first sequence;

~~(c)~~ (i) examining whether the first and second sequences can be extended to include neighboring nucleotides by checking complementarity between corresponding neighboring nucleotides of each of the first and second sequences;

~~(d)~~ (j) extending each of the first and second sequences by one nucleotide when complementarity is found in step ~~(c)~~ (i);

~~(e)~~ (k) repeating steps ~~(c) and (d)~~ (i) and (j) in both directions of the first and second sequences until complementarity is not found;

~~(f)~~ (l) determining the sequences thereby selected;

~~(g)~~ (m) repeating steps ~~(b) through (f)~~ (h) through (l) starting at a different region from that already selected in step ~~(b)~~ (h) until all complementary second sequences for said first sequence have been selected; and

~~(h)~~ (n) repeating steps ~~(a) through (g)~~ (g) through (m) for all possible first sequences on the target mRNA or its precursor without selecting the same pair more than once.

11. (Currently Amended) The method of claim 8, wherein said numerical value is expressed as $((L+1)/r)^F \cdot \exp(|\Delta G|/RT)$, wherein ΔG is the bond energy for forming a complementary double-stranded region, R is the gas constant, T is the absolute temperature, L is an integer from 3 to 10, r is one plus the number of nucleic acid bases between said first target region and said complementary region, with the provision that ~~$r>L+1$~~ $r \geq L+1$, and F is a positive number not greater than 6.

12. (Previously Presented) The method of claim 11, wherein $|\Delta G|$ is determined by the nearest neighbor model.

13. (Previously Presented) The method of claim 11, wherein L is 4 to 6.

14. (Previously Presented) The method of claim 11, wherein L is 4.

15. (Previously Presented) The method of claim 11, wherein F is 6.

16. (Previously Presented) The method of claim 11, wherein L is 4 to 6, and $|\Delta G|$ is determined by the nearest neighbor model.

17. (Previously Presented) The method of claim 11, wherein L is 4, and $|\Delta G|$ is determined by the nearest neighbor model.

18. (Currently Amended) A method for designing an antisense oligonucleotide sequence for a target mRNA or its precursor comprising the steps of:

(a) selecting a first sequence consisting of 2 or more nucleotides in the target mRNA or its precursor;

(b) selecting a second sequence that is complementary to the first sequence that is separated by at least three nucleotides from the first sequence;

(c) examining whether the first and second sequences can be extended to include neighboring nucleotides by checking complementarity between corresponding neighboring nucleotides of each of the first and second sequences;

(d) extending each of the first and second sequences by one nucleotide when complementarity is found in step (c);

(e) repeating steps (c) and (d) in both directions of the first and second sequences until complementarity is not found;

(f) determining the sequences thereby selected;

(g) assigning a numerical value to said sequences that reflects the possibility of forming a complementary double-stranded region between said sequences based upon the distance between said sequences and the bond energy ΔG for said sequences, wherein a lower numerical value indicates a lower possibility, and wherein the numerical value increases with an increase in said bond energy and the value decreases with an increase in the distance between said paired sequences;

(h) assigning the numerical ~~value~~ values obtained in step (g) to each nucleotide of each of the sequences;

(i) repeating the steps (b) through (h) starting with different region from that already selected in step (b), until all allowable second sequences for said first sequence have been selected;

(j) repeating steps (a) through (i) for all possible first sequences on the target mRNA or its precursor without selecting the same pair more than once;

(k) summing the numerical values, which are assigned in step (h) for all sequences selected in steps (a) through (j), for each nucleotide in the mRNA or its precursor;

(l) selecting one or more regions each of which ~~consist~~ consists of at least 6 contiguous nucleotides and have a low summed value relative to another region; and

(m) designing [[an]] one or more antisense ~~oligonucleotide~~ oligonucleotides, wherein each oligonucleotide is complementary to ~~said~~ a region selected in step (l).

19. (Currently Amended) The method of claim 18, wherein said numerical value is expressed as $((L+1)/r)^F \exp(|\Delta G|/RT)$, wherein ΔG is the bond energy for forming a complementary double-stranded region, R is the gas constant, T is the absolute temperature, L is an integer from 3 to 10, r is one plus the number of nucleic acid bases between said first target region and said complementary region, with the provision that ~~r>L+1~~ $r \geq L+1$, and F is a positive number not greater than 6.

20. (Previously Presented) The method of claim 19, wherein $|\Delta G|$ is determined by the nearest neighbor model.

21. (Previously Presented) The method of claim 19, wherein L is 4 to 6.

22. (Previously Presented) The method of claim 19, wherein L is 4.

23. (Previously Presented) The method of claim 19, wherein F is 6.

24. (Previously Presented) The method of claim 19, wherein L is 4 to 6, and $|\Delta G|$ is determined by the nearest neighbor model.

25. (Previously Presented) The method of claim 19, wherein L is 4, and $|\Delta G|$ is determined by the nearest neighbor model.